Citation:

Rockell JE, Williams SM, Taylor RW, Grant AM, Jones IE, Goulding A. Two-year changes in bone and body composition in young children with a history of prolonged milk avoidance. *Osteoporos Int.* 2005 Sep;16(9):1016-23. Epub 2004 Nov 23.

PubMed ID: 15565350

Study Design:

Longitudinal Study

Class:

C - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To determine:

- whether or not the children had increased their milk and dietary calcium intakes since baseline visit 2 years prior
- to find out whether they exhibited any catch-up in height, bone area, and total and regional bone mineral accrual relative to a reference population of milk-drinking children from the same community

Inclusion Criteria:

- Participants from the study conducted 2 years prior
- Must have been in that previous study to be considered for this one
- Must still be residing in Dunedin and be willing to do this follow-up study

Exclusion Criteria:

No other criteria described.

Description of Study Protocol:

Recruitment

- Must have participated in the previous study visit (baseline) 2 years prior to be recruited for this follow-up study visit
- Baseline study subjects were recruited from advertisements placed in shops, schools and community well-child clinics

Design: Longitudinal study

- Questionnaires on general health, physical activity, nutrition, bone health and body composition measured
- Information concerning beverage consumption of the children and parental height was also collected at follow-up visit
- Pubertal status was assessed in children over 8 years of age
- Current calcium intakes were estimated both by the same FFQ used at baseline and by 4 day diet records

Blinding used (if applicable):

The same scanner (Lunar DPX-L) was used for baseline and follow up scans, which were taken and analyzed by the same person using the Lunar Software package.

Intervention (if applicable): not applicable

Statistical Analysis

- Analyses performed with Strata 7.0
- Data presented as means±standard deviation and ranges
- Anthropocentric and bone measures are expressed as Hz scores derived from a contemporary reference population of 100 boys and 100 girls who had no history of fracture and lived in Unending

Data Collection Summary:

Timing of Measurements

- 4 day diet records (4DDRs) were collected just before the follow-up clinic appointment to avoid post-interview bias
- The 4DDRs were collected on three randomly selected non-consecutive weekdays and one weekend day

Dependent Variables

- Anthropometry - weighed and measured in light clothing
- Body mass index (BMI) calculated as weight in kilograms divided by height in meters squared
- Body composition and bone mineral density was measured by dual x-ray absorptiometry (DXA)
- Four DXA scans (total body, left hip, lumbar spine and non dominant forearm) were performed according to the recommendations of the manufacturer

Independent Variables

- Current calcium intake assessed by a validated food-frequency questionnaire (FFQ)
- Use of alternative substitute calcium-rich beverages or mineral supplements was assessed by questionnaire
- Mean daily nutrient composition of the children's diets was calculated from the 4DDRs with the "Diet Cruncher" program and computerized New Zealand food composition database

Control Variables

Description of Actual Data Sample:

Initial N: Baseline visit consisted of 50 Caucasian children aged 3-10 years

Attrition (final N): 28 girls, 18 boys completed the follow up study

- The remaining 2 girls and 2 boys from the original sample had gone overseas and could not be contacted
- One participant seen at follow-up did not complete the 4DDR

Age: 5-12 years old, mean 8.1 ± 2.0 years

Ethnicity: Caucasian

Other relevant demographics:

Anthropometrics

- 41 children were Tanner Stage 1
- 3 girls were Tanner Stage 2
- 2 girls were Tanner Stage 3

Location: Dunedin

Summary of Results:

Key Findings

- Thirteen children (28.3%) had history of fracture, with 5 new fractures occurring during the 24 months follow-up
- At follow-up, adverse symptoms to milk had diminished and modest increases in milk consumption and calcium intake had occurred.
- At follow-up current calcium intakes from all sources were positively correlated with the Z scores for total body BMC ($r=0.34$, $P<0.023$), total bone area ($r=0.33$, $P<0.025$), ultradistal radial BMD ($r=0.36$, $P<0.014$) and 33% radial BMD ($r=0.30$, $P<0.045$).
- For every additional 100mg of calcium consumed was commensurate with a change of approximately 0.1 unit of the Z score for each of these.
- However, although some catch-up in height had taken place, the group remained significantly shorter than the reference population, with elevated BMI.
- The ultradistal radius BMC Z scores remained low.
- The Z scores for BMD had improved to lie within the normal range at predominantly cortical sites (33% radius, neck of femur and hip trochanter) but had worsened at predominantly trabecular sites (ultradistal radius and lumbar spine), where values lay below those of the reference group ($P < 0.05$).
- Similarly, although volumetric BMAD Z scores at the 33% radius had normalized, BMAD Z scores at the lumbar spine remained below the reference population at follow-up (-0.67 ± 1.12, $P < 0.001$).
- From baseline to 24 months, time reported for vigorous physical activity (min/day) decreased from median 46, range 8-197 to a median of 77, range of 0-197
- 12 subjects (26%) rated their physical activity for age and gender as below average

- When study subjects are compared to children of similar age from the reference population:
  - 26(22) vs 56(65) in girls P<0.02
  - 41(26) vs 86(44) in boys P<0.001
- Principal reasons reported for avoiding milk:
  - 30 subjects stated lifestyle choice or taste dislike
  - 16 stated adverse symptoms were the reason for avoidance
- Symptoms reported related to milk:
  - 22 participants reported symptoms at baseline but only 10 at follow-up listed one or more symptoms
    - 8 of those 10 had GI problems
    - 2 reported rhinitis or respiratory problems
    - 4 reported dermatitis
    - 5 reported headaches, glue ear or malaise that were attributed to drinking milk

	Baseline Mean (SD)	Follow-up Mean (SD)	2-year change Mean (95% CI)
Height (cm)	-0.74(1.33)[aa]	-0.39(1.14)[a]	0.35(0.20,0.51)[b]
Weight (kg)	0.01(1.14)	0.18(1.22)	0.16(0.06,0.27)[b]
BMI (kg/m^2)	0.51(0.90)[aa]	0.46(1.00)[aa]	-0.06(-0.20, 0.09)
Lean Mass (kg)	-0.18(1.13)	-0.02(1.08)	0.16(0.03, 0.28)[b]
Fat Mass (kg)	0.09(1.03)	0.29(1.14)	0.19(0.02,0.36)[b]
Total body BMC (kg)	-0.44(1.11)[a]	-0.19(1.06)	0.25 (0.14,0.37)[b]

[a] P<0.05, [aa]P<0.01 significantly different from reference population (z-test)

[b]P<0.05 significant change from baseline (paired t-test)

Author Conclusion:

Our results demonstrate persisting height reduction, overweight and osteopenia at the ultradistal radius and lumbar spine in young milk avoiders over 2 years of follow-up.

Reviewer Comments:

It is noted in the discussion that milk in New Zealand is not supplemented with vitamin D and that lack of vitamin D is detrimental to bone development.

They also note that most of the children in this study were breast fed for prolonged periods and it is likely the transition to cow's milk during their 2nd year of life was particularly difficult, giving them low protein and calcium intakes.

This study only looks at Caucasian children and early milk avoidance may be less detrimental to bone development in other groupsso further research is needed.

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes

2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	???
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes

5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	N/A
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	N/A
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes

8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	???
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	???
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	No